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CLINICAL REVIEW

Assessment of respiratory effort during sleep: Esophageal pressure versus noninvasive monitoring techniques

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S U M M A R Y

Monitoring of respiratory effort is paramount in the clinical diagnostic recording of sleep. Increased respiratory effort is a sign of obstructive sleep-disordered breathing and is associated with arousals from sleep. Respiration is the result of muscle activity that induces negative intrathoracic pressure and expansion of the thoracic and abdominal cavities. Therefore respiratory effort may be recorded from mechanical, electrical and electromechanical signals. Several techniques are available for the recording of respiratory effort. Monitoring of esophageal pressure is still the method of choice, as the pressure signal directly reflects the respiratory muscle force. However, esophageal pressure monitoring is cumbersome and may be replaced with noninvasive techniques. In order to be reliable, these techniques must be validated against the esophageal pressure standard. The present review presents a concise description of the technical principles and, if available, a comparison with esophageal pressure data, based on a systematic literature search. Most data are available on respiratory inductance plethysmography, and confirm that this technique is suitable for routine diagnostic investigation of respiratory effort during sleep. Pulse transit time, diaphragmatic electromyography, snoring loudness, suprasternal pressure monitoring, midsagittal jaw movement and forehead venous pressure monitoring are promising alternative techniques although only limited validation is available.

Introduction

Respiratory disorders of sleep are quite common. In contemporary medical practice, advanced diagnostic tools are employed to characterize the nature of sleep-disordered breathing (SDB). Whilst the monitoring of respiratory effort is paramount, different and sometimes disparate monitoring techniques are being used for this purpose. The present review aims to concisely describe the various methods for physiological measurement of respiratory effort in the pathophysiological framework of obstructive SDB. Arousal from sleep is a key feature of obstructive SDB, and therefore, the relation between respiratory effort and arousal is discussed first. A major part of this review deals with noninvasive monitoring techniques and their significance with respect to (invasive) esophageal manometry, which is recognized as the gold standard for the assessment of respiratory effort. Based on a systematic literature search, it was assessed whether existing noninvasive methods have been validated against measurement of esophageal pressure.

Note that the characterization of respiratory effort in central sleep apnea is outside the scope of this paper.

Obstructive respiratory events and arousals in sleep

Obstructive sleep apnea, hypopnea and respiratory effort related arousals

To denote a condition with recurrent events of upper airway (UA) narrowing and impaired airflow during sleep, the term obstructive sleep apnea (OSA) is commonly used [1]. In this context, 'apnea' itself means complete closure of the UA with cessation of airflow, whereas 'hypopnea' refers to a partial obstruction of the UA with reduced airflow. According to current scoring criteria, these events last at least 10 s in adults, whereas in children they should

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Abbreviations

AASM	American Academy of Sleep Medicine
EMG	electromyography
FVP	forehead venous pressure
OSA	obstructive sleep apnea
Pes	esophageal pressure
PPG	photoplethysmography
PTT	pulse transit time
RERA	respiratory effort related arousal
RIP	respiratory inductance plethysmography
SDB	sleep-disordered breathing
UA	upper airway
UARS	upper airway resistance syndrome

encompass two or more disrupted breaths [2]. Ongoing and usually increasing inspiratory effort is the hallmark of obstructive SDB [3]. Typically, termination of these events is associated with a transient arousal from sleep, during which UA dilating muscles are activated, UA patency is restored, and airflow resumes [4]. In 1999, Guilleminault and co-workers for the first time associated arousal from sleep with peak esophageal pressure in patients with excessive daytime sleepiness but no apparent sleep apnea, and coined this disorder the upper airway syndrome (UARS) [5]. In more recent years, further attention has been drawn on subtle obstructive breathing events that are associated with increased respiratory effort, but no obvious or only slight reduction in airflow. As these events are also associated with an arousal, they are called 'respiratory effort-related arousals' (RERAs) [6].

UARS is a form of SDB characterized by the predominant presence of RERAs. As a clinical condition, however, it is currently subsumed under the diagnosis of OSA [1].

The relation between respiratory effort and arousals

Increasing respiratory effort preceding arousal from sleep is a key factor in the pathophysiology of OSA. Vincken et al. observed that during obstructive apneas the force of the diaphragm increases progressively with each occluded inspiratory effort, to reach a point at which arousal from sleep occurs [7]. This level of inspiratory force was found to approximate the threshold of muscle fatigue. A close temporal relationship was observed between this critical point, onset of arousal and opening of the UA. Gleeson et al. examined the mechanisms underlying the arousal response to respiratory strain in sleep [8]. In eight healthy men, arousal-inducing effects of different respiratory challenges were studied, including added inspiratory resistive load, hypoxia, and hypercapnia. In agreement with the observations of Vincken et al., it was found that the appearance of arousal events was primarily linked to increasing respiratory effort. The peak-negative esophageal pressure at inspiration prior to arousal, whilst different between individuals, was consistently reproducible within each individual under the various stimulus conditions. These results corroborated the hypothesis that increasing ventilatory effort is the final common pathway to arousal from sleep, irrespective of the mechanisms that incite the rising drive to breathe. It was postulated that pulmonary and/or thoracic mechanoreceptors may be involved in the arousal mechanism [8]. Alternatively, it is conceivable that the central respiratory drive, rather then the peripheral mechanonoreceptor input may be the primary mechanism that triggers the arousal [9].

More recently, it was reported that the temporal association between the onset of arousal and the restitution of breathing is variable among OSA patients [10]. Younes investigated 82 OSA patients and provoked UA obstruction by dial-down of continuous positive airway pressure. In 17% of the induced obstructive respiratory events, there were no arousals at all, whereas in 22% resumption of breathing preceded the onset of arousal by 0.5–12.0 s. While these findings would challenge the concept that arousing from sleep is an indispensable mechanism in the termination of UA obstruction, they do not invalidate the fact that the vast majority of obstructive respiratory events are associated with arousals, regardless of their role in restoring the patency of the UA.

Other authors have emphasized the importance of UA mechanoreceptors in OSA [11,12]. Pressure-sensing mechanisms play a prominent role in modulating upper airway neuromuscular activity during wakefulness and sleep. A negative pressure reflex within the upper airway serves to stabilize the upper airway during inspiration. Impairment of this reflex may predispose to OSA [12]. Application of local anesthesia to the UA increases apnea duration, suggesting that suppression of UA mechanoceptor activity impairs the arousal response to obstructive breathing [13]. In an investigation on the relation between increased UA resistance and arousal, it was observed that flow limitation is invariably present in respiratory-related arousals, and often precedes rises in respiratory effort [14]. In this study, which involved normal subjects in whom alcohol was used to increase upper airway resistance, increased respiratory effort preceded arousals in only 23% of the respiratory events. This finding would imply that other mechanisms than increased respiratory effort are associated with sleep interruption in normal subjects under certain conditions. Indeed, susceptible non-apneic individuals might awaken easily from sleep by mere stimulation of UA receptors, whereas this mechanism may be blunted and forceful inspiratory effort may be required to cause arousal from sleep as the severity of SDB progresses over time.

Measurement of respiratory effort

As respiratory effort is paramount in the pathophysiology and operational definition of OSA, its measurement is an integral part of the standard polysomnography montage. The revised manual for the scoring of sleep and associated events by the American Academy of Sleep Medicine (AASM) recommends the use of esophageal manometry, or dual thoracoabdominal respiratory inductance plethysmography for this purpose [2,15]. Esophageal pressure (Pes) monitoring is the technique of choice, because the pressure signal directly reflects the respiratory muscle force. As it is an invasive method, it is faced with problems of poor acceptance and tolerability. Moreover, there are concerns that an indwelling catheter in the UA could modify pharyngeal dynamics [16]. It has been suggested that Pes monitoring may negatively affect sleep quality [17,18]. Most sleep centers do not routinely employ this technique, because it is quite cumbersome and expensive. For these reasons, it would be preferable to use noninvasive monitoring techniques as they are better accepted by patients. Several alternative methods for monitoring respiratory effort are available to date. They are based on physiological signals related to breathing activity, including thoraco-abdominal movement, pulse transit time (PTT), respiratory sound, electromyography (EMG) of the respiratory muscles, suprasternal pressure, jaw movement, and venous pressure. The fundamental question is, however, whether these techniques can measure respiratory effort as reliably as Pes monitoring?

Research methods

PubMed and Cochrane central register were searched up to September 2014, using a combination of MeSH terms and free text.

The flowchart of the literature search and data extraction is presented in Fig. 1.

First, all papers dealing with sleep apnea syndrome were identified using either “obstructive sleep apnea”, “obstructive sleep apnea”, “sleep related respiratory disorder”, “sleep disordered breathing”, “sleep apnea syndromes”, OSAS, OSA, SHS, OSAHS, apnea, apnea, hypopnea or hypopnea as search terms. Second, a subset of papers was identified using the following terms: esophagus, esophagus, “esophageal pressure”, “esophageal manometry”, “oesophageal pressure”, “oesophageal manometry”, “pulse transit time”, PTT, plethysmography, “respiratory inductance plethysmography”, RIP, diaphragm, “diaphragm EMG”, “intercostal EMG”, suprasternal, “suprasternal pressure”, snoring, “crescendo snoring”, “midsagittal jaw movement”, “jaw movement”, mandible, “mandible movement”, JAWAC, “forehead venous pressure” or “venous pressure”. The selection was limited to papers published after 1964 in English, Dutch, French or German. This initial search yielded 114 hits.

The abstracts of the publications from the initial search were screened to retrieve original research papers that specifically dealt with the topic of measuring respiratory effort and that compared one or more noninvasive techniques with Pes monitoring.

The following exclusion criteria were applied: i) no original data (reviews, editorials); ii) studies not addressing the comparison between Pes monitoring and non-invasive techniques to monitor respiratory effort; iii) studies not in humans.

Relevant publications were checked with respect to prior and subsequent citations in the literature using Web of Science®. Any additional articles that could be identified with this procedure were also considered eligible for the present review and were selected using the same methods. In this additional search, no supplementary articles were found.

The eligibility of each abstract or full-text article was assessed in a standardized manner by the first author. Doubts about the eligibility of an abstract or full-text were resolved by consensus among the reviewers. Information extracted included year of publication, country of data collection, study design, validity outcomes and sample characteristics.

In total, seven papers were found that met the aforementioned criteria.

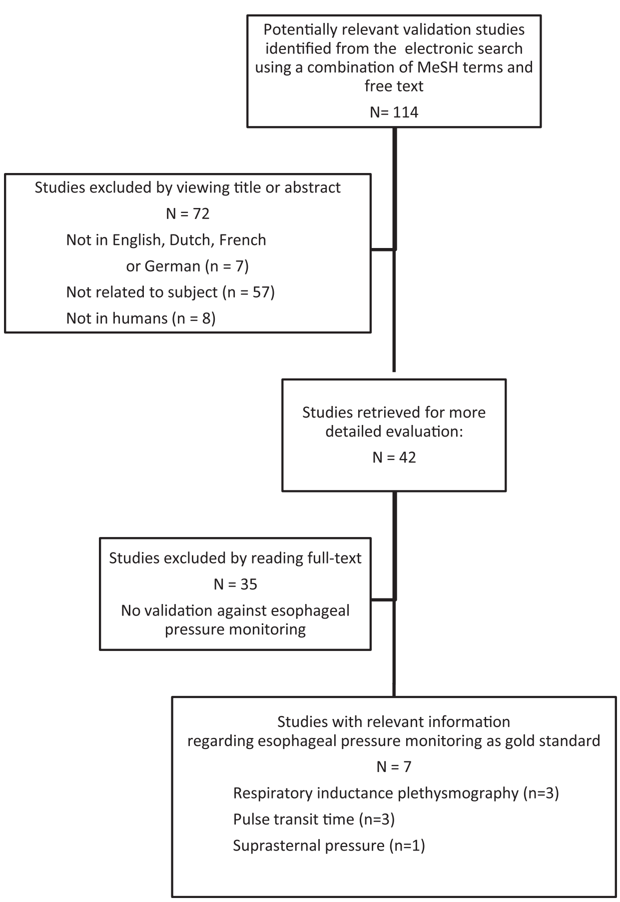

Fig. 1. Flow chart of literature search.

Esophageal pressure monitoring

As yet, Pes monitoring is the gold standard for the measurement of respiratory effort. Pleural pressure changes, generated by respiratory muscle force, are transmitted to the organs inside the thoracic cavity, including the esophagus. Therefore, pleural pressure changes can be validly measured by an indwelling catheter in the esophagus [19]. Different devices are available for esophageal manometry, including air-filled balloon-tip catheters, fluid-filled catheters, and solid state pressure sensors [20]. The choice, placement and management of Pes catheters is outside the scope of this review. The reader is referred to Kushida et al. for an exhaustive technical protocol on the use of Pes monitoring [21].

The increased respiratory effort associated with obstructive respiratory events (‘Pes event’) and the return to baseline upon arousal (‘Pes reversal’) can be accurately demonstrated with Pes monitoring [6]. A crescendo respiratory effort associated with arousal from sleep can easily be observed in many obstructive apneas, hypopneas and is by definition present in all RERAs (Fig. 2). Guilleminault and Chowdhuri have empirically identified three other Pes-associated respiratory patterns that are associated with arousals: a) increased Pes, without crescendo, terminated by a Pes reversal; b) one or two breath increases in Pes preceding a Pes reversal; and c) tachypnea with normal Pes, abruptly terminated by a normal breath [22]. Many other Pes-associated patterns have been described in the literature and have been used to define respiratory events [14,23–34] (Table 1). Obviously, there is no uniform definition of Pes events and it may be anticipated that different types exist in different patient populations [35]. There is some evidence that subtle sequences of increased respiratory effort may play a role in SDB observed in children [36] and non-obese women [37]. Clearly, future research will have to point out whether such patterns are clinically relevant and if they have implications for the present definition of obstructive respiratory events.

Noninvasive monitoring of respiratory effort

Respiratory effort is reflected in various physiological phenomena, and may be monitored from mechanical, electrical and electromechanical signals.

Ventilation is the result of 1) contraction of respiratory muscles inducing 2) expansion of the thorax and abdomen and 3) negative intrathoracic pressure. The first phenomenon may be assessed by EMG of the diaphragm or intercostal muscles, the second directly by Pes monitoring or indirectly by measuring suprasternal pressure, PTT, respiratory sound or venous pressure, and the third directly by thoracoabdominal plethysmography or indirectly by gauging jaw movements.

Nasal pressure is particularly useful to demonstrate UA obstruction. Increasing UA resistance is associated with flow limitation, which is visible from the nasal pressure signal as a flattening of the otherwise rounded inspiratory curve [38]. Flow limitation is

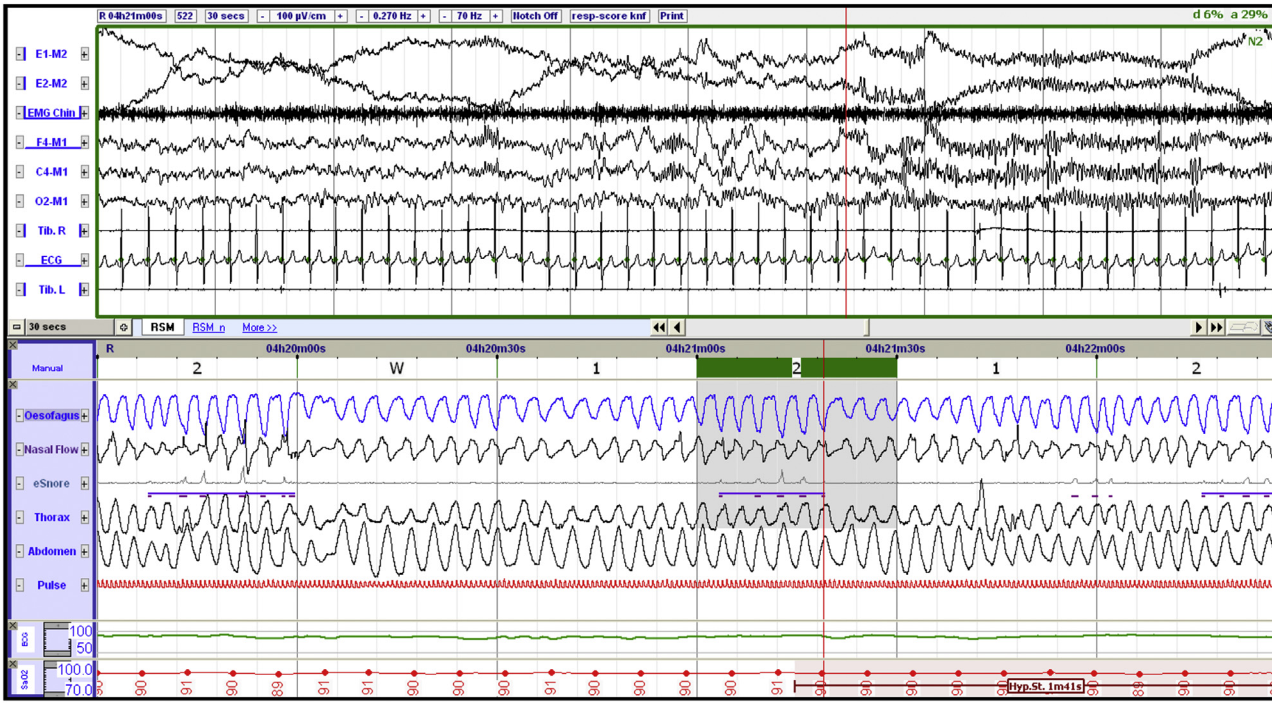

Fig. 2. Esophageal pressure event (Pes event) with crescendo respiratory effort, arousal and esophageal pressure reversal (Pes reversal). Sleep recording showing three Pes events (underlined in purple colour) indicated by flow limitation (nasal flow channel) and snoring (E-snore channel). During these events inspiratory esophageal pressure swings increase (esophagus channel). In the subsequent Pes reversal, hallmarked by an arousal in the EEG, inspiratory pressure swings and inspiratory flow contours return to baseline. Pes = esophageal pressure, EEG = electroencephalography.

indicative of elevated UA resistance, but is not a direct sign of increasing respiratory effort. As such, nasal pressure is outside the scope of this review and will not be addressed any further.

The various indices of respiratory effort are presented below. Most investigations have dealt with thoracoabdominal plethysmography and PTT. Other techniques lack appropriate validation and will be discussed under miscellaneous methods.

Thoracoabdominal plethysmography

Monitoring technique

In routine clinical practice, recording of thoracoabdominal excursions is used for the assessment of respiratory movement. Expansion of the thoracic and abdominal compartments can be monitored by sensors sensitive to longitudinal tension, e.g., strain gauges and belts with piezoelectric sensors. These sensors reflect changes in one dimension, i.e., length. Respiratory inductance plethysmography (RIP) is a technique based on measurement of electrical inductance. RIP sensors are embedded in bands that are placed separately around the thorax and the abdomen. Variations in inductance reflect changes of the entire cross-sectional area enclosed by the bands [15]. Because the vertical dimensions of thorax and abdomen do not vary with respiration, RIP actually reflects changes in volume of these two compartments [39]. Following calibration of the thoracic and the abdominal bands by means of a reference-volume device (pneumotachograph or spirometer), lung ventilation may be estimated fairly accurately [40,41]. Therefore, RIP is preferred over the use of strain gauges.

A practical problem of RIP is that the calibration status depends on the position of the bands around the thorax and abdomen. Displacement of the bands due to changes in body position during sleep may alter calibration settings and the volumes measured [42,43]. Despite this drawback, RIP is recommended by the AASM as the preferred method for monitoring respiratory effort in routine clinical polysomnography [2,15].

The sum of the thoracic and abdominal RIP signals allows detection of a relative change in tidal volume compared to baseline breathing, even without calibration of the signals [15].

Of note, a phase shift of thoracoabdominal movements is a sign of obstructive respiration, which may be associated with a reduction in tidal volume [31]. The magnitude of the RIP signals may or may not be proportional to the variations in Pes excursions.

Validation of RIP against Pes monitoring

Until present, three studies have been conducted to assess RIP against Pes monitoring on the basis of predefined Pes events [24,31,34] (Tables 2a and 2b). All studies were carried out in middle-aged patients with UARS or mild OSA (AHI $\leq$ 10/h). Whilst different methods and definitions were used, overall sensitivity of RIP was adequate, with values varying between 0.84 and 0.94. Specificity, assessed in two studies [24,31] was $\geq$0.90. Intra- and interobserver variability, assessed in two studies [31,34] was $\geq$0.80. Therefore, RIP seems to be a reliable method to noninvasively detect increased respiratory effort and to identify associated obstructive respiratory events. However, it has as yet not been explored whether RIP is also useful to gauge the degree of inspiratory effort, as indicated by the nadir of negative pressure swings assessed with the Pes monitoring technique.

Pulse transit time

Monitoring technique

Pulse transit time is the time interval ($t_2 - t_1$) for a pulse wave to travel between two places (p_1 and p_2) in the arterial system. The speed at which this wave moves is proportional to the arterial tone or stiffness, which is in turn determined by the arterial blood

Table 1
Definition of respiratory events and related esophageal pressure events according to specific patterns observed during esophageal pressure monitoring in obstructive sleep apnea.

Aricle, reference number	Definition of respiratory events	Definition of Pes events
Tvinnereim M et al. 1995 [23]	A: not available H: not available	A crescendo pattern for >10 s after at least one stable epoch
Loube DI et al. 1999 [24]	A: absence of oronasal thermistor signal for ≥10 s H: ≥ 50% decrement in oronasal signal for at ≥10 s associated with evidence of increasing respiratory effort measured by qualitative inductive plethysmography	If the most negative Pes exceeded the baseline wake minimum negative Pes by 50% and was ≤ −12 cmH_2O
Ayappa I et al. 2000 [25]	A: decrease in peak inspiratory signal to below 10% of the surrounding baseline for ≥10 s H: decrease in airflow to less than 50% of the baseline for two or more breaths (usually >10 s)	A crescendo pattern for at least 10 s followed by a rapid decrease to basline level
Watanabe T et al. 2000 [26]	A: cessation of signal H: >50% decrease of signal	A drop of Pes nadir by more than 13.5 cmH_2O
Guilleminault C et al. 2001 [27]	A: international criteria H: decrease of the nasal cannula mouth thermistor signal by at least 50% of amplitude compared to just prior to recording lasting for at least 10 s, and associated with either an arousal or a drop in oxygen desaturation of at least 3%	1) Increased Pes, without crescendo, terminated by a Pes reversal 2) One or two breath increases in Pes preceding a Pes reversal 3) Tachypnea with normal Pes, abruptly terminated by a normal breath
Bachour A et al. 2002 [28]	A: cessation of signal for ≥10 s H: reduction of >50% in signal for ≥ 10 s and an arousal or an oxygen saturation drop of ≥3%	A crescendo pattern lasted for 10 s or longer and ended with a sudden return to baseline. The minimal increase in the negative esophageal pressure at the end of the esophageal event was at least 5 cmH_2O or more than 50% of the baseline level
Poyares D et al. 2002 [29]	A: absence of signal for ≥10 s H: reduction of ≥30% in signal for ≥10 s	A more negative peak end inspiratory Pes on three successive breaths compared to prior breathing, terminated with an abrupt shift of at least 25% of the peak negative end inspiratory Pes toward less effort (Pes reversal)
Katz ES et al. 2003 [30]	OA: the presence of chest/abdominal wall motion associated with a ≥80% reduction in the thermistor signal, a loss of end-tidal PCO_2 waveform, Pes swings and paradoxical respiratory efforts lasting the duration of ≥two breaths OH: similar to OA, except that the reduction in thermistor signal was 50–80% of baseline and was associated with drop an oxygen saturation drop of ≥4% and/or arousal	A crescendo pattern lasting ≥10 s and ending in an abrupt Pes reversal
Masa JF et al. 2003 [31]	A: absence of oronasal thermistor signal of ≥10 s H: oronasal thermistor signal decreased ≥30% for ≥10 s with an oxygen saturation drop of ≥4% or final arousal	Increasing negative Pes in the two or more breaths prior to an arousal and Pes becomes less negative in the arousal
Hutter DA et al. 2004 [32]	A: cessation of signal for ≥10 s H: 1) reduction of signal for ≥50% and an oxygen saturation drop of ≥3% for ≥10 s 2) reduction of signal for ≥ 20% and an oxygen saturation drop of ≥3% for ≥10 s	Decrescendo-crescendo pattern with a nadir > −10 cmH_2O
Johnson PL et al. 2005 [14]	A: absence of signal ≥10 s H: a clear amplitude reduction of a validated measure of breathing for ≥10 s, and associated with either an oxygen desaturation of >3% or an arousal	At least one breath of increased negative Pes, EEG arousal, and a return to less-negative Pes
Stoohs RA et al. 2005 [33]	A: absence of signal ≥10 s H: reduction of ≥30% in signal ≥10 s	A minimum number of three inspiratory efforts
Masa JF et al. 2009 [34]	A: absence of oral-nasal thermistor signal ≥10 H: discernible reduction in thermistor signal for ≥10 s with ≥3% oxygen desaturation or final arousal	An increase in Pes with both desaturation and/or arousal

A = apnea, EEG = electroencephalography, H = hypopnea, OA = obstructive apnea, OH = obstructive hypopnea, Pes = esophageal pressure.

pressure. Rises in arterial tension are associated with a shortening of the PTT, whereas a fall in blood pressure will cause the PTT to prolong [44].

Since decreases in pleural pressure during obstructed breathing are accompanied by drops in systolic blood pressure (pulsus paradoxus) [45], inspiratory effort may also be reflected by rises in PTT [46]. In addition, peaks in arterial tension that come with arousals at the end of obstructive respiratory events are hallmarked by a drop in PTT [47].

The pulse wave is actually kicked off by the opening of the aortic valve. Although there is a slight time interval between the electrocardiographic R wave and this event, corresponding to the isometric contraction of the ventricle, the R wave is taken as the temporal starting point (t1) of the pulse wave. The end point (p2) is the arterial vascular bed of the fingertip. A photoplethysmographic sensor placed on this site captures the pulse wave, and the terminal time point (t2) is by convention located on the ascending part of this wave at 25 or 50% of the zenith. The time between the R-wave of ECG and the detection of the pulse wave on the fingertip varies between 200 and 250 ms. Thus, reproducible PTT measurements can be made with every heart beat, simply by using the ECG and a plethysmographic probe on the fingertip.

There are some limitations to this technique [44]. First, the frequency of measurements is equal to the pulse rate (0.6–2.0 Hz), which is below the sampling frequency required for adequate recording of the respiratory cycle (≥5.0 Hz) [48]. Because of this limitation, there is a clear tendency for PTT to undersample the respiratory effort wave form, as a consequence of which the actual peaks and troughs of the ventilatory cycle may be missed. Furthermore, the signal may become irregular during REM sleep due to the instability of the autonomous nervous system and the erratic changes in blood pressure. Finally, interpretation of PTT is seriously hampered in patients with cardiac arrhythmias such as atrial fibrillation.

Table 2a
Respiratory effort related events assessed by respiratory inductance plethysmography in comparison with esophageal pressure monitoring. Characteristics of trials validating respiratory inductance plethysmography against esophageal pressure monitoring.

Article, reference number	N (%M)	Mean age, years ± SD	Mean AHI ± SD or (range), events/h	Mean BMI ± SD, kg/m^2	N (events)	Comparison
Loube DI et al. 1999 [24]	UARS (n = 9) Non-UARS (n = 5) (% M not specified)	UARS: 38 ± 6 Non-UARS: 35 ± 10	3 (0–6)	UARS: 27.3 ± 1.7 Non-UARS: 27.1 ± 3.1	n.a.	Correlation between change in peak inspiratory flow to mean inspiratory flow ratio and change in Pes
Masa JF et al. 2003 [31]	94 (81% M)	44.5 ± 9.5	4.6 ± 5.9	28 ± 4	14,617 arousals	Correlation between RERA index determined by Pes and RIP.
Masa JF et al. 2009 [34]	90 (81% M)	44 ± 10	3.9 ± 5.4	28 ± 4	3767 NI-ONEs 4148 OP-ONEs	An increase in Pes with both desaturation and/or arousal compared with a discernible decrease in the thoracoabdominal motion ≥10 s, followed by a ≥3% oxygen desaturation and/or arousal

AHI = apnea hypopnea index, BMI = body mass index, M = male, N = number, n.a. = not available, NI-ONE = obstructive nonapneic event using noninvasive method (respiratory inductance plethysmography), OP-ONE = obstructive nonapneic event using esophageal pressure, Pes = esophageal pressure, RERA = respiratory effort related arousal, RIP = respiratory inductance plethysmography, SD = standard deviation, UARS = upper airway resistance syndrome.

Table 2b
Respiratory effort related events assessed by respiratory inductance plethysmography in comparison with esophageal pressure monitoring. Sensitivity, specificity and predictive values of trials validating respiratory inductance plethysmography against esophageal pressure monitoring.

Article, reference number	Sensitivity (95%CI)	Specificity (95%CI)	PPV (95%CI)	NPV (95%CI)	Intraobserver agreement	Interobserver agreement
Loube DI et al. 1999 [24]	0.84 (0.67[a]–1.00[b])	0.90 (0.80[a]–1.00[b])	n.a.	n.a.	n.a.	n.a.
Masa JF et al. 2003 [31]	0.94 (0.93[c]–0.94[d])	0.94 (0.95[c]–0.93[d])	0.90 (0.91[c]–0.89[d])	0.94 (0.92[c]–0.94[d])	0.80	0.85
Masa JF et al. 2009 [34]	0.93 (0.98[e]–0.89[f]–0.91[g])	n.a.	n.a.	n.a.	0.89 (0.96[e]–0.82[g])	0.88 (0.90[e]–0.86[g])

CI = confidence interval.
n.a. = not available.
NPV = negative predictive value.
PPV = positive predictive value.
[a] Stage-2 sleep.
[b] Immediately prior to arousal.
[c] Group with sleepiness.
[d] Group without sleepiness.
[e] Event + desaturation.
[f] Event + arousal.
[g] Event + arousal or desaturation.

Validation of PTT against Pes monitoring

Individual PTT values correlate poorly with absolute blood pressure, and therefore also with absolute intrathoracic pressure values. However, in three studies in OSA patients, reasonable correlations were found between the amplitude of PTT oscillations (ΔPTT) and the magnitude of negative pleural pressure swings assessed with Pes monitoring [29,48,49] (Tables 3a and 3b). Overall sensitivity of PTT was adequate, with values varying between 0.80 and 0.93. Specificity and interobserver variability were not assessed in all studies, and were inconsistent among studies. Therefore, the PTT seems to offer a (semi)quantitative estimate of inspiratory effort, but is not a valid surrogate marker for Pes monitoring.

Miscellaneous methods

Several alternative techniques are available for the monitoring of respiratory effort. This section provides a concise description of the various methods and includes some data on clinical usefulness. None of these techniques, however, has been validated against Pes monitoring.

Diaphragm electromyography and intercostal electromyography

Monitoring the electric activity of the diaphragmatic and intercostal muscular system is the most direct way to obtain information on respiratory muscle function [50]. Technically, standard surface electrodes are placed in pairs in the intercostal space on the right anterior chest (intercostal EMG) or ion the right anterior axillary line in the seventh and eighth intercostal spaces (diaphragmatic EMG) [33]. It requires some experience and skills to obtain a legible signal as EMG recordings are prone to artefact and the electrocardiographic signal is usually superimposed.

EMG recordings can be useful for differentiating central, obstructive, and mixed breathing events. Incremental respiratory effort is readily apparent from the EMG trace, even if the signal is

Table 3a
Respiratory effort related events assessed by pulse transit time in comparison with esophageal pressure. Characteristics of trials validating pulse transit time against esophageal pressure monitoring.

Article, reference number	N (%M)	Mean age, years ± SD	Mean AHI ± SD, events/h	Mean BMI ± SD, kg/m^2	N (events)	Comparison
Argod J et al. 1998 [49]	13 (100%M)	47.3 ± 14.1	25.1 ± 16.6	27.1 ± 4.5	167	A crescendo trend in Pes versus a clear increase in oscillations in PTT
Argod J et al. 2000 [48]	9 (100%M)	49 ± 10	25.1 ± 10.8	25.9 ± 3.5	340	A crescendo in Pes versus increase in oscillations in PTT
Poyares D et al. 2002 [29]	20 (75%M) UARS: 10 OSAS: 10	UARS: 39.7 ± 8.6 OSAS: 46.5 ± 10.0	UARS: 2.7 ± 2.1 OSAS: 15.3 ± 8.1	UARS: 29.3 ± 5.8 OSAS: 29.6 ± 5.6	UARS: 389 OSAS: 779	Pes crescendo terminated by Pes reversal versus a fall in PTT curve of 15 ms

M = male, N = number, OSAS = obstructive sleep apnea syndrome, Pes = esophageal pressure, PTT = pulse transit time, SD = standard deviation, UARS = upper airway resistance syndrome.

Table 3b
Respiratory effort related events assessed by pulse transit time in comparison with esophageal pressure. Sensitivity, specificity and predictive values of trials validating pulse transit time against esophageal pressure monitoring.

Article, reference number	Sensitivity (95%CI)	Specificity (95%CI)	PPV (95%CI)	NPV (95%CI)	Intraobserver agreement	Interobserver agreement
Argod J et al. 1998 [49]	0.93 (0.94–0.91)	0.96 (0.97–0.95)	0.95 (0.96–0.94)	0.94 (0.95–0.92)	n.a.	0.95
Argod J et al. 2000 [48]	0.80	n.a.	0.91	n.a.	n.a.	0.37
Poyares D et al. 2002 [29]	0.90	0.22	0.83	0.36	n.a.	n.a.

CI = confidence interval, n.a. = not available, NPV = negative predictive value, PPV = positive predictive value.

not calibrated. Diaphragmatic EMG has been compared with but not validated against Pes monitoring [33]. Normalized data showed a good correlation between the two measures during apneas and hypopneas. It was found that the percentage increase in Pes and diaphragmatic EMG during obstructive events corresponded well, and that the percentage increase was higher in apneas as compared with hypopneas [33]. At present, there are no comparative studies with intercostal EMG, and neither diaphragmatic EMG nor intercostal EMG have been formally validated against Pes monitoring.

Respiratory sounds: snoring

Snoring is basically an inspiratory sound, although sometimes an expiratory component can be heard. Snoring is a salient sign of obstructive SDB: in obstructive apneas snoring is observed in between the respiratory events, whereas in obstructive hypopneas snoring is present during the events and may show an incremental pattern, reflecting the crescendo respiratory effort [51]. The relation between the degree of negative inspiratory esophageal pressure and snoring loudness has been evaluated in only two studies. Stoohs et al. monitored snoring sound intensities in non-apneic habitual snorers with daytime hypersomnolence [52]. Although regression analysis of Pes and snoring sound intensities indicated positive interdependence in all subjects, there were important differences in the slope of the correlation. Itasaka et al. found a relation between the logarithmic transformation of the intra-esophageal pressure amplitude and the intensity of snoring in the supine and lateral decubitus positions [53]. In a recent study by Norman et al., a new and promising noninvasive technique is described for measuring respiratory effort on the basis of crescendo snoring [54]. To date, there are no formal studies that validate snoring intensity against Pes monitoring.

Suprasternal and supraclavicular pressure monitoring

Published data are available on the monitoring of suprasternal and supraclavicular pressure. In a first investigation, a microphone was embedded in a cuff and was placed over the trachea in the sternal notch [55]. This device was used as a pressure transducer. Provided that the cuff was adequately sealed to the skin to ensure an airtight cavity, changes in intrathoracic pressure were converted into a legible signal of respiratory effort. Using this technique, Meslier et al. found a very good concordance with Pes for the detection of obstructive apneas, with a sensitivity of 99.4% and a specificity of 93.6% [55]. However, no data were made available on inter- and intrascorer reliability.

Second, results have been published from a study using a piezoelectric stretch sensor (OptiflexTM UAR®, Sleepmate Technologies, VA, USA) attached onto the supraclavicular fossa [14]. The signal from this device is a sinusoidal waveform, corresponding to respiration, which enlarges with increasing inspiratory effort. Johnson et al. used this technique along with Pes monitoring to discern respiratory effort from flow limitation as primary conditions associated with arousal from sleep. It was found that flow limitation preceded all of the respiratory arousals, whereas an increase in the size of the piezoelectric sensor signal was present in only 40% of these events, indicating a low sensitivity [14]. Moreover, 86% of the Pes events were correctly identified from the piezoelectric sensor signal. Unfortunately, this piezoelectric device was not properly validated against Pes monitoring. Therefore, the usefulness of supraclavicular pressure monitoring as a surrogate marker for respiratory effort remains to be determined.

Midsagittal jaw movement analysis

It has been observed that during obstructive SDB the jaw is lowered with each inspiration, and that this movement is proportional to the inspiratory effort [56]. The pathophysiological mechanism is not entirely clear, but it may be assumed that increasingly negative intrathoracic pressure may be transmitted to the jaw via caudal traction upon the central airways and, consequently, that jaw movements could reflect the effort to breathe [57]. Mandibular opening can be measured meticulously by magnetometry (JawSens®, Nomics, Angleur, Belgium) [58]. The sensor is made of two coupled resonant circuits, placed perpendicularly to the midline of the face, on the forehead and below the lower lip. The output voltage is a cubic function of distance. The mandibular movement signal can be expressed either in absolute value (mm) or in normalized value (percentage of mouth opening). Recently data have been published on the inter- and intrascorer reliability of different respiratory events identified by mandibular movements [59]. Although Pes monitoring was used in this study, formal validation against Pes monitoring was not performed.

Until present, no validation studies against Pes monitoring have been performed.

Forehead venous pressure (FVP)

Photoplethysmography (PPG) of the skin is increasingly being used to monitor circulatory and respiratory functions. It has been shown that intensity variations of the PPG signal may be induced by respiration [60]. Although the physiological background of respiratory-induced intensity variations is not fully understood, it is assumed that the fluctuation of venous return to the heart, linked to the alterations in intrathoracic pressure, is a dominant mechanism [61]. The peak-to-peak amplitude of these respiratory-induced intensity variations is closely correlated with tidal volume and respiratory changes in peripheral venous pressure. PPG applied to the forehead is believed to monitor respiration-related changes of volume or pressure in the veins of the skin. Using a commercial device (ARES™ Unicorder, Advanced Brain Monitoring, Carlsbad, CA), PPG has been applied in a trial to validate forehead venous pressure (FVP) as a measure of respiratory effort for the diagnosis of sleep apnea [61]. The monitoring of FVP is based on a composite signal derived from optical, motion and pressure sensors. Appropriate filters are used to optimize the resultant signal in different conditions. The study was designed to assess face validity of the FVP against established measures of respiratory effort, i.e., Pes monitoring, thoracic RIP and abdominal RIP. Two qualified scorers evaluated 200 respiratory events obtained from polysomnography in 14 subjects with suspected sleep apnea. The inter-rater Kappa scores across all event types indicated all four effort signals provided moderate agreement ($\kappa = 0.43$–0.47). Pes monitoring and FVP provided better inter-rater agreement in the detection of both obstructive hypopneas and apneas as compared with the RIP variables. The Kappa scores for the intra-rater

comparison of the four effort signals showed near perfect agreement ($\kappa = 0.81–0.86$). The results of this study would suggest that the FVP can serve as an alternative to other measures of respiratory effort. Yet, no final conclusions can be drawn regarding this new technology, as additional studies are needed to confirm its reproducibility and validity with respect to Pes monitoring.

Conclusions

Monitoring of respiratory effort is an essential part of standard polysomnography. Increasing respiratory effort is a basic feature of obstructive sleep-disordered breathing, since it indicates obstruction and is related to arousal from sleep at the end of the respiratory events. Traditionally, it was considered that these arousals constitute the main mechanism of apnea termination. Recently, some doubt has been casted on this concept as the temporal relationship between the ending of obstructive events and the arousals may be variable. In some events no arousals are observed at all. On the other hand, some respiratory arousals may only be preceded by flow limitation and not by increased respiratory effort. To identify the respiratory nature of arousals, technically accurate measurement of respiratory effort is mandatory. Respiratory effort is characterised by muscular activity of the diaphragm and intercostal muscles, changes in intrathoracic pressure and volume expansion of the trunk. Any of these physiological phenomena may serve as a source for measurement of respiratory effort. Esophageal pressure monitoring is still the reference method, because this technique allows direct assessment of the amplitude of the muscle force. Because esophageal pressure monitoring is invasive, other techniques are needed for routine diagnostic investigations. To date, most validation studies have been carried out in RIP and PTT. As these investigations have primarily focused on mild forms of OSA, the diagnostic value of these tests in more severe disease remains uncertain.

Respiratory inductance plethysmography of thorax and abdomen is currently the best studied and most valuable alternative. Although inductance plethysmography reflects variations of volume rather than muscle force, it is advocated by the AASM as a suitable method for monitoring respiratory effort in clinical sleep recordings. The use of other techniques is limited by the fact that they have been insufficiently investigated, are inaccurate or have not been validated against the reference method.

Practice points

1. Esophageal pressure monitoring is still the reference method to monitor respiratory effort.
2. Because esophageal pressure monitoring is invasive, other techniques are needed for routine diagnostic investigations.
3. Pulse transit time, diaphragmatic electromyography, snoring loudness, suprasternal pressure monitoring, midsagittal jaw movement and forehead venous pressure monitoring are alternative noninvasive techniques, but only limited validation data are available.
4. Respiratory inductance plethysmography of thorax and abdomen is currently the best studied and most valuable alternative to measure respiratory effort.

Research agenda

1. Noninvasive alternatives to esophageal pressure for the assessment of respiratory effort should be systematically validated against Pes monitoring.
2. Although respiratory inductance plethysmography is clinically useful, the technique is not the best model for muscle force as it gauges volume expansion. Methods assessing pressure changes are more suited, and warrant further exploration.
3. Noninvasive assessment of the degree of negative intrathoracic pressure with increasing respiratory effort should actually be the prime goal of novel technologies for monitoring of respiratory effort. This parameter has been shown to predict the threshold for arousal, as the peak-negative intrathoracic pressure level preceding arousal, whilst different between individuals, is consistently reproducible within individuals.
4. It is currently unknown whether variant patterns of respiratory effort in obstructive sleep-disordered breathing have a different pathophysiological meaning. There is a need to gather information in large groups of sleep apnea patients of different genders and age categories on the types of respiratory pressures that can be observed.
5. There is an opportunity for signal processing engineers to focus on this issue and to devise a composite signal derived from different sensors to model the shape and magnitude of intrathoracic pressure swings.

Conflict of interest

The authors do not have any conflicts of interest to disclose.

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